

REMARKS

First, applicants wish to thank the examiner for the courtesies extended during the interview conducted on September 10, 2008. As discussed at the interview, applicants provide a declaration from Dr. Braithwaite with exhibit slides. The Braithwaite declaration explains the nature of the problems (both generally known and not generally known) encountered in soft tissue replacements in the orthopedics field, the prior art attempts at solving these problems, the differences between the claimed invention and the prior art, and the numerous advantages provided by the claimed invention over the prior art. The Spiegelberg declarations filed previously also are relevant to this discussion.

In this amendment and request, paragraph numbers refer to the specification as published in 20040171740A1. Applicants have deleted the priority claim as per MPEP § 201.11(III)(G). Claims 135-156 are now pending in this application. Claims 1-134 are cancelled without prejudice or disclaimer. These claims supersede and replace the claims filed on July 1, 2008 without prejudice or disclaimer. Support for the claims presented herein can be found throughout the application. Applicants point out exemplary support for the new claims below:

Support for "contacting" and "controlled" can be found at paragraphs [106], [111], [115], [121], and [154]. Support for "mixing" can be found at paragraphs [15], [20], [23], and [196]. Support for "workable" can be found at paragraphs [195-98]. Absence of chemical cross-linkers, irradiation or thermal cycling is discussed at paragraph [115].

Physical crosslinking is discussed at paragraph [132]. Anisotropy is discussed at paragraph [127]. Figures 21A and B are flow diagrams of exemplary methods of preparing injectable solutions and the resulting *in situ* hydrogels. Thetagels are an injectable solution and are discussed at paragraphs [30-35], [44-46], [50], [55], [65-67], [106-10], [129-32], [152] and [167-76], and more specifically refer to when the Flory interaction parameter, which is dictated by temperature, solvent, and polymer (e.g., PVA) is such that the polymer prefers to be with the solvent rather than itself. With the introduction of the second solution, the Flory interaction parameter increases, causing the PVA polymer chains to move towards each other and overcome the 'solvation force,' causing localized phase separation, with regions having high concentrations of polymer (precursors to junction points) and regions with low concentrations (precursors to pores). See Figure 2. If this localized phase separation is controlled appropriately, [106-112] and [121], the polymer chains can align to form crystalline junction points (crosslinks), which sets up a three-dimensional porous structure of polymer with some absorbed water, with the pores filled with water (*i.e.*, a hydrogel). If this phase separation occurs too quickly, the polymer precipitates out of solution (crashes out) before the polymer chains have an opportunity to form crystalline junction points or distinct precursor zones (junction points and pores), and consequently it will not over time form a hydrogel. paragraph [106]

The claims are enabled and definite

Without acquiescing in any rejection, applicants have replaced the previous claims with claims 135-156. Support for the claims in the specification and an explanation of terms is set forth above. Applicants therefore submit that the Section 112 rejections are moot, and should be withdrawn. During the interview, the examiner agreed that the new claims would overcome the Section 112 rejections.

The claimed invention is not taught or suggested by the prior art

The examiner has rejected the previous claims over various combinations of Hyon, Yamauchi, Tanihara, Ku, Yao and Okamura. Applicants have provided in depth arguments to distinguish these references, and therefore will summarize these arguments below.

- Ku, Yao, Hyon, and Okamura all require freezing step to form a hydrogel. See Ku *et al.* (see claim 1), Yao (see claim 1), Hyon (see claim 1) and Okamura (see the "constitution"). Yamauchi *et al.* states in its "constitution" that ionized radiation is used to form a gel. See Tests 2 and 3 of the Spiegelberg declaration (February 13, 2008). Therefore, to achieve injection of a hydrogel according to these references, the body space would have to be subjected to ionizing radiation or reduced in temperature below 0°C. See also Braithwaite declaration at paragraph 18.
- Tanihari discloses the use of a co-polymer, not a vinyl polymer, for use in a wound dressing. See Tests 2-3 and paragraph 5 of the Spiegelberg declaration (February 13, 2008). To obtain a hydrogel, Tanihara employed: (1) cross-linking

with radiation or peroxides; (2) cooling the solution; (3) freezing of the solution; and (4) repetition of freezing and thawing. See column 20, line 15 of Tanihara. In additional, Tanihara methods require either chemical reaction of the polymer solution with an anhydride or taurine, or a freeze-thaw process. None of these approaches would allow for injectability. See also Braithwaite declaration at paragraph 18.

In contrast to these references, the claimed invention requires none of these steps and, in fact, specifically recites "wherein the polymer hydrogel is formed without chemical crosslinkers, irradiation or thermal cycling." The invention provides for an injectable thetagel solution that will gel *in situ* to form the hydrogel without the need for deleterious treatments of the body. See the Braithwaite Declaration at paragraphs 10-17.

The Federal Circuit has held that the citation of many references which skirt around the invention is indicative of patentability, not obviousness. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 93 (Fed. Cir. 1986); *see generally In re Herrick*, 145 USPQ 400, 402 (CCPA 1965). Applicants submit that this principle applies here, and therefore urge that the rejections be withdrawn.

The claimed invention has unexpectedly improved properties and characteristics, and satisfies a long-felt but previously unmet need

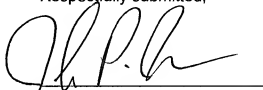
As explained in paragraph 3 of the 2008 Spiegelberg declaration and paragraph 19 of the Braithwaite declaration, the claimed invention unexpectedly provides and allows for (1) minimally invasive surgery, (2) a porous, highly hydrated system allows fluid and nutrient flow from endplates, (3) space-filling for optimal load-transfer to the annulus fibrosis, (4) the absence of chemical action, so there are no unwanted chemical by-products or exothermic (heat) occurrences, (5) no need for ionizing radiation or thermal cycling, so the hydrogel can form within, and fill and conform to the body space. This is achieved while satisfying the long-felt need for an injectable product. See MPEP § 2141.

The attainment of unexpected results or properties is a powerful demonstration of patentability. See *U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Lindemann Maschinenfabrik v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1461 (Fed. Cir. 1984). Absent evidence to the contrary, applicants' demonstration of unexpected results further establishes patentability. See *In re Soni*, 34 USPQ2d 1684, 1687-88 (Fed. Cir. 1995). Furthermore, The satisfaction of long-felt need constitutes further evidence of the patentability of the present invention. See *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). These objective indicia of non-obviousness further demonstrate the patentability of the invention.

REQUEST

Applicants submit that claims 135-156 are in condition for allowance and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,



John P. Isacson
Reg. No. 33,715

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PROSKAUER ROSE LLP
1001 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Phone: 202-416-6800
Fax: 202-416-6899
Customer No. 61263